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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant: Marvin L. Schilling et al  
Serial No: 09/964,120  
Filed: 09-25-2001  
For: Method for Producing Biologically Active Products  
Group Art Unit: 1616 Examiner: Sharmila S. Gollamudi

Hon. Commissioner of Patents  
& Trademarks,  
Washington, D.C. 20231

Brief under 37 CFR 1.192

Appellants in the subject application herewith appeal from the decision of the Examiner finally rejecting claims 42 to 51. In accordance with the provisions of 37 CFR 1.192 appellants state:

Real Party. That they, the inventors, Marvin L. Schilling and Richard D Fafard are the real party in interest.

Related Matters. There are no other appeals or interferences known to appellants relating to the subject matter of this application.

Status of Claims. Claims are pending in this appeal, a copy of which is attached hereto.

Status of Amendments. Appellants' amendment of the claims in response to the 35 USC 112 objections in the final rejection has been entered for purposes of this appeal and is attached.

Summary of Invention. This invention relates to a method of thermally dehydrating Type II collagen containing cartilage by combining such in comminuted form with at least 15 % by weight of the cartilage of an ionizing salt such as potassium chloride and an antimicrobial agent, heating the resulting mixture at temperatures that will prevent denaturization, more specifically set forth in the dependent claims as below 110<sup>0</sup> F, until the water content is reduced to less than 15 % to obtain a product that contains at least 45 % by weight of the cartilage of the salt and also retains the original, organic (i.e., other than water) structure of the cartilage, and particularly the Type II collagen .

Issues.

Group 1

(1) The rejection of the claims 42 - 51 as unpatentable under 35 USC 103 over Moore (US 5,645,851) in view of Ueno et al (US 4,789,497) or in view of JP 59025637, optionally in further view of Puppolo (US 5,562,535).

(2) The propriety of the combination of references.

Group 2

(3) The rejection of Claim 51 as unpatentable under 35 USC 103 over Moore (US 5,645,851) in view of JP 59025637 in further view of JP 59-088065

(4) the propriety of the combination.

Grouping of Claims. The rejections are applicable to all claims on appeal in Group 1 and applicable only to claim 51 in Group 2.

(8) Argument.

The process of the present invention relates to the thermal dehydration of bone cartilage that contains the protein, Type II collagen, in the presence of an antimicrobial agent and an ionic salt at temperatures below which denaturization occurs. The denaturization is defined as any change in the original organic structure of the material being dehydrated. The dehydration is conducted until the water content is reduced so that it is no longer subject to pathogenic contamination during a period of commercially attractive shelf life and is set forth in the claims as below 15 % of the weight of the cartilage. In order to retain the original structure during the dehydration process, appellants not only use temperatures which are known not to denature the organic structure of the cartilage, but also employ massive amounts of an ionic salt, which is combined with the comminuted cartilage itself, in addition to an antimicrobial agent. The dehydrated product has a salt content of at least 45 %. Claim 43 sets forth the use of the salt in solid form. Claim 44 sets forth a numerical upper temperature limit. Claim 45 further defines the antimicrobial agent. Claim 46 further limits the antimicrobial agent of claim 45 to a hypochlorite. Claim 47 defines the ionizable salt as either potassium or sodium chloride. Claim 48 further defines the salt content of the final product. Claims 49 through 51 incorporate limitations of the earlier dependent claims and further limit the scope of the invention to chicken cartilage.

The examiner misconstrues appellants' invention in order to make the prior art fit by ignoring the fact that the present invention and the claims call for the presence of the salt during the dehydration step and not during any washing step. The reduction of the water content of the cartilage to below 15 % without denaturing the organic components of the cartilage, and particularly the Type II collagen, is achieved by the presence of the large concentration of salt during dehydration and that is the essence of the invention defined by the claims.

Claims 42 – 51 have been rejected under 35 USC §103(a) as unpatentable over Moore (US 5,645,851) in view of Ueno et al (US 4,789,497) or in view of JP 59025637 and optionally further in view of Puppolo (US 5,562,535).

Claim 51 has also been rejected as unpatentable under 35 USC §103 over Moore (US 5,645,851) in view of JP 59025637 in further view of JP 59-088065.

Rejection of Claims 42-51 over Moore in view of Ueno

The Moore reference discloses the thermal dehydration of chicken cartilage and points out that exposing the Type II collagen containing materials to boiling water or acid solutions causes the material to become denatured. Moore teaches that it is essential to maintain the insoluble nature of the Type II collagen in order to retain its biological activity and prevent denaturization, which is defined in the patent as the breakdown of the polymeric structure of the Type II collagen causing it to become soluble in water (Column 2, lines 6-19 and column 3, lines 18 –35). In the examples Moore discloses dehydration at 60<sup>0</sup> C (140<sup>0</sup> F) (column 7, line 8), and at an average temperature of 110<sup>0</sup> F, which includes both temperatures above and below 110<sup>0</sup> F (column 7, line 19). Thus Moore contains no suggestion that the drying temperatures used would cause the Type II collagen to denature and suggest to one skilled in the art that the procedures employed in the reference should be modified. There is no appreciation for the specific temperature limit found by appellants to be necessary to prevent denaturing the Type II collagen protein. More importantly there is no suggestion that the drying process should be carried out in the presence of the substantial quantities of an ionizing salt to prevent the Type II collagen from denaturing.

The Ueno et al reference (Ueno) relates to the dehydration of fish meat. The fish meat is not disclosed as containing Type II collagen or for that matter of any collagen. The Ueno invention involves the washing of fish meat using a solution containing two types of ionic salts. The salts are added to the wash water in a concentration of 0.05 to 5 wt. %. The washed fish meat is then dehydrated by mechanical squeezing that reduces

the water content from 95 % down to 85 to 72 %. The object of the washing step is to remove “factors” which might cause denaturation of proteins during freezing and the object of the addition of the salt is to reduce the swelling of the fish meat during washing (column 1, lines 16 –30) and thus limit the addition of water to the fish meat during washing.

Appellants submit that the examiner has failed to show the necessary suggestion, teaching or motivation to combine these two references and that the combination is based on a hindsight analysis of the claimed invention. The law as pronounced by the Court of Appeals of the Federal Circuit is very clear that the examiner must show suggestion, teaching or motivation to combine references as an essential element of an obviousness holding (Brown Williamson Tobacco Corp. v. Phillips Morris Inc., 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed.Cir. 2000)). In In re Dembiczak, (175 F.3d 994, 999, 50 USPQ2d 1225, 1232 (Fed.Cir. 1999)) the Court stated: “Our case law makes clear that the best defense against the subtle but powerful attraction of hindsight based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references”. In re Fine (837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed.Cir. 1988)) the holding was that “teachings of references can be combined only if there is some suggestion or incentive to do so” (emphasis in original). Most recently the Court held in In re Lee (277 F.3d 1338, at 1342, 61 USPQ2d 1430 at 1433 (Fed.Cir. 2002)

“The factual question of motivation is material to patentability and could not be resolved on subjective belief and unknown authority. It is improper, in determining whether a person of ordinary skill in the art would have been led to this combination of references simply to “[use] that which the inventor taught against the teacher”.----- Thus the Board must not only assure that the requisite findings are made based on the evidence of record but must also explain the reasoning by which the findings are deemed to support the agency’s conclusion.”

The dehydration process of Ueno differs from the claimed process in that: (a) it does not involve the same type of material or the same type of protein being dehydrated and the examiner has not shown any evidence supporting equivalence, (b) it does not involve the same type of dehydration mechanism and again the examiner has not shown

any evidence supporting equivalence, (c) it does not involve the same type of denaturization and again the examiner has not shown any evidence supporting equivalence, (d) it does not involve the same extent of dehydration and again the examiner has disregarded this difference and (e) the examiner has failed to show that the salt concentrations employed in the reference during dehydration are anywhere close to those employed in appellants' process or result in products having the salt concentrations set forth in appellants' claims.

Both Moore and Ueno are strictly limited to the particular materials dehydrated. Given the vast array of proteins known to persons skilled in the art and their different properties there has to be some thread that connects the cartilage of Moore with the fish meat of Ueno other than appellants' teachings. None has been suggested. Nothing in Moore furthermore suggests any alternate form of dehydration and nothing in Ueno suggests heating as a means to remove water. On the contrary Ueno wants to prepare a frozen product and not a dry product and principally only water absorbed during the washing is removed. Ueno seeks to improve taste and mechanical properties of the frozen and thawed fish meat (see Examples 3 and 4) and is not concerned with any health benefits of proteins. Since the references do not provide a basis for their combination the decisions of the Court of Appeals of the Federal Circuit would require the examiner to cite evidence that would cause a person skilled in the art to combine these two references, but none has been cited. Moore teaches in Example 11 the grinding of cartilage in the presence of liquid nitrogen,  $-196^{\circ}\text{C}$ , (column 6, lines 62-68) without any apparent effect on the efficacy of the Type II collagen. In Ueno the purpose of the process is to minimize the denaturization of the fish meat during freezing thus indicating either different proteins or different type of denaturization, in either event there is no evidence suggesting that Ueno's teachings are applicable to Moore..

The combination of Moore with Ueno when tested against the standard required by the Court of Appeals for the Federal Circuit in In re Lee is therefore unjustified and the rejection should be reversed. Thus the examiner has not made the requisite factual

finding that would permit the combination and has failed to explain the reasoning that would support the combination..

Furthermore even if the teachings of Ueno could be relied on, the obviousness rejection still would not be justified. The examiner bases her rejection on the single statement in the reference that it is well known that the addition of a salt at the time of washing improves dehydration, without taking the remainder of the reference into consideration. The examiner uses this statement totally out of context of its meaning in the reference. In order to find obviousness the examiner has made “dehydration” synonymous with “denaturization”, and ignores the fact that salt can be and is used for purposes other than to prevent denaturization in dehydration, which is how it is used in Ueno. Thus, the patentees disclose that denaturization resulting from freezing is prevented by washing the fish meat to remove factors causing such denaturization (column 1, line 17 – 20). This makes it clear that the denaturation involved in the Japanese patent is not the same as that involved in appellants’ process, where nothing is removed from the cartilage either before or during dehydration other than water. The salt is added to the wash water in Ueno not to prevent denaturization but to reduce the swelling of the fish meat as the result of the washing, which otherwise would also cause elution of desirable material from the fish meat. Thus a closer examination of the record demonstrates that even though salt may be present during dehydration, and that is debatable, it is not present to prevent denaturization. Certainly the quantities of salt employed in appellants’ process have not been demonstrated to be present during the dehydration and a person skilled in the art would know that such could not be present based on just having up to 5 % of salt dissolved in the water used to wash the fish meat prior to dehydration. Thus the sentence as relied on by the examiner does not support the assertion that it would be obvious to add salt to prevent denaturization as a result of heating Type II collagen containing cartilage in a dehydration process based on heating.

The examiner argues that Ueno would make it obvious to add the salt to the washing step of Moore and come up with appellants’ invention. But there is no disclosure that Moore has any swelling problem with the cartilage that he is washing or

that washing would cause denaturization. The concentration of the salt disclosed in the wash water of Ueno is from 0.5 to 5%. Even if one skilled in the art would find a reason to add the salt of Ueno to the wash water of Moore, the most it would show is that the cartilage came in contact with salt, but there is no evidence of any amount the dissolved salt being retained by the cartilage and there is no suggestion that would lead to the high concentrations employed in appellants' invention during dehydration and in the final product.

Appellants submit that the combination of Moore with Ueno fails to make obvious the claims of the present invention.

Rejection of Claims 42-51 over Moore and JP 59035637

The Examiner has further in the alternative rejected the claims as unpatentable over the combination of Moore with Japanese Patent abstract 59035637. The examiner cited this reference in the final office action asserting it was necessitated as a result of new issues raised by appellants' amendment of the claims. However the only changes made by appellants to the claims were to incorporate limitations set forth in dependent claims into the independent claim. Since the examiner rejected all of the claims and therefore considered all of the claims no new issues could have been generated. However since the reference is no closer than the art cited or more relevant, appellants respond to the rejection.

The Japanese abstract discloses the dehydration of shell ligaments and edges of scallops "using" 7-15 % salt. They are then mixed with cuttle fish liver which also previously had been dehydrated with 7 to 15 % salt. Although it might be argued that the salt concentration in the products of the reference and in appellants' claims overlap at the 15 % level, they are not disclosed as overlapping in the dehydrated product and nothing in the reference suggests such.



The examiner asserts that the ligaments contain Type II collagen, however no support or evidence for such has been cited. It is appellants understanding that ligaments comprise Type I collagen. The reference contains no disclosure that would suggest that the ligaments involved contain any Type II collagen. Appellants submit that the examiner has failed to lay a foundation for the combination.

No reason for the use of the salt in the dehydration is given, nor is there any disclosure of how the dehydration is to be conducted and to what extent water is removed. Thus the dehydration could be merely the addition of the salt to draw water hygroscopically out of the scallop ligaments or it could be a mechanical dehydration to squeeze out minor amounts of water as shown for example by Ueno discussed above. In neither event would a dried product be obtained that had water contents of less than 15 % and salt contents above 45 %. Nothing in the reference relates to achieving dehydration by heating the material nor is there any suggestion of preventing denaturization of any proteins contained in the ligaments. The Examiner has failed to cite any suggestion teaching or motivation why a person skilled in the art would combine the abstract with the Moore reference. Any obviousness argument thus is based on using appellants' teachings and based on hindsight.

#### Rejection in view of Puppolo

Claims 42 to 51 have also been optionally rejected in view of foregoing combinations of references and in view of Puppolo. The examiner cites the Puppolo reference, as stated in the response to the final action, to demonstrate the inherent features of Moore.

Puppolo relates to a process for drying shark cartilage to "spare the potential denaturing of its biologically active proteins". The actual process involves as a first step the proteolytic digestion of the shark cartilage to remove the protein. The solution is accomplished by treating the cartilage with a solution of hydrochloric acid or acetic acid also containing a proteolytic enzyme. The proteolytic digestion appears to be squarely

contradictory to the stated purpose spare denaturing of biologically active proteins. This is then followed by an azeotropic extraction to remove some of the water. Suitable solvents for such azeotropic extraction include benzene, toluene, hexane, and heptane. The remainder of the water, now containing also the organic solvent, is then removed in a sonic drier at temperatures of 85<sup>0</sup> F.

Again the examiner picks out pieces of the reference without considering the entire teachings. The examiner ignores the fact that the reference relates to an azeotropic extraction involving the use of an organic solvent to combine with the water. Thus water is removed as a mixture with an organic solvent and it is because of using the organic solvent that Puppolo is able to obtain a dry product at low temperatures. Moore dries the product at higher temperatures and at most Puppolo suggests that Moore might want to use azeotropic distillation in his drying procedures to do so at lower temperatures, but nothing in Moore suggests that drying without a solvent is inadequate. Since the drying steps of the two processes are very different and rely on different principles there can be no inherent results in Puppolo that are applicable to Moore.

Puppolo subjects his raw product to a proteolytic digestion involving the use of a proteolytic enzyme in an acid solution (column 2, lines 13-19) to remove protein. Such treatment would be destructive of the undenatured, insoluble Type II collagen and form the less desirable soluble Type II collagen disclosed by Moore in column 3, lines 28-31. It is not clear what proteins Puppolo removes by this technique but most certainly it would lead one skilled in the art away from using the Puppolo drying method if one wanted to maintain the Type II collagen in the original undenatured form.

Puppolo contains no disclosure of the use of salt during the drying process and thus is not seen to overcome the failure of the combinations of art discussed above to make appellants' claims obvious.

The rejection of claim 51 over Moore in view of Ueno or JP59025637 in further view of JP 59-088065

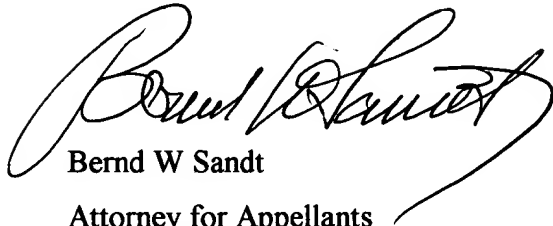
Claim 51, which modifies the drying procedure of the chicken cartilage of claim 49 by adding either lecithin or hydroxy propyl methyl cellulose or lecithin to the mixture of the cartilage and salt. The purpose of the lecithin is to prevent the material to stick to the walls of the dryer. This claim has been rejected over the combination of Moore with either Ueno or the Japanese patent abstract as discussed above and further in view of another Japanese patent, JP 59-088065. The examiner relies on the second Japanese reference to show the use of lecithin during dehydration.

The '59 Japanese patent discloses a process in which comminuted bone and marrow of animals is combined with an aqueous alkaline solution of lecithin and a solution of sodium hypochlorite and then pulverized to an ultra-fine powder at temperatures of  $-15^{\circ}\text{C}$ , which is stated to prevent denaturation. The product is then soaked and washed and dehydrated by mechanical means such as a centrifugal separator. No reason is given as to why the lecithin is added to the comminuted bone and marrow before it is pulverized at  $-15^{\circ}\text{C}$ . The washing of the pulverized product leaves in doubt the presence of any of the lecithin in the product when it is dehydrated.

It is not seen where this reference would suggest the addition of lecithin to a thermal dehydration. Thus the lecithin is added to a cold pulverization step in the reference and even if any of the lecithin is present in the pulverized product when it is dehydrated by mechanical means there is no reason for a person skilled in the art to extend such disclosure to a thermal dehydration process. Appellants' claim is therefore deemed to be patentable over this combination of references.

Furthermore if the independent claim from which claim 51 depends is held to be patentable, dependent claim 51 would also be held patentable. Appellants in their initial argument here have demonstrated the patentability of the independent claim.

Appellants request that the examiner's rejection be vacated and the claims be held allowable.



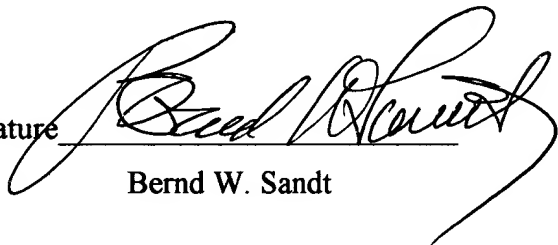
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Certificate under 37 CFR 1.8

I hereby certify that three copies of the foregoing brief together with a check for the necessary fees is being deposited with the United States Postal Service by Express Mail ER04272303 US, addressed Mail Stop: Appeal Brief-Patents, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, as of the date set forth below.

Date: May 12, 2004

Signature   
Bernd W. Sandt



### Claims on Appeal

42. A method for the dehydration of Type II collagen containing cartilage in its natural form, which comprises,
- (a) combining said cartilage with an antimicrobial agent and at least 15 % by weight of the cartilage of an ionizing salt,
  - (b) heating the resulting mixture in particulate form at a temperature below which denaturization of the Type II collagen occurs until the water content is reduced to below 15 % by weight of the cartilage, and
  - (c) recovering a product containing the collagen II-containing protein of the cartilage in its original form and having a salt content of at least 45 % by weight of the cartilage.
43. The method of claim 42 wherein the ionizing salt is used in solid form.
44. The method of claim 42 wherein the heating is conducted at a temperature below about 110° F.
45. The method of claim 42 wherein the process is carried out in the presence of an oxygen containing antimicrobial agent and an ionizable consumable salt.
46. The method of claim 45 wherein anti-microbial agent is a hypochlorite.
47. The method of claim 42 wherein the salt is sodium or potassium chloride.
48. The process of claim 42 in which the salt concentration in the dried product is from 45 to 60% of the cartilage.
49. The method of dehydrating chicken cartilage containing Type II collagen in its natural form which comprises
- (a) comminuting said cartilage,

- (b) soaking the resulting product in an aqueous solution of an antimicrobial agent, and blending such with potassium or sodium chloride in a concentration of at least 15 % by weight of the comminuted product,
- (c) dehydrating the resulting mixture in particulate form at temperatures below 110<sup>0</sup>F until the water content of the mixture is reduced to below 10%, and recovering a product containing the Type II collagen of the chicken cartilage in its natural form and having a salt content of 45 to 60 % by weight of the cartilage.

50. The method of claim 49 wherein the antimicrobial agent is a hypochlorite.

51. The process of claim 39 wherein the dehydration is carried out in the presence of hydroxy-propyl methyl cellulose or lecithin.